UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,072	01/15/2002	Ralph M. Steinman	MER-011CN/112917-144	7452

43852 7590 11/29/2005

MERIX BIOSCIENCE, INC.
4233 TECHNOLOGY DRIVE
DURHAM, NC 27704

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,072	STEINMAN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2005 and 19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 9/19/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks, filed 6/23/05, have been entered.

2. Claims 1-6 and 10-12 are being acted upon.

3. In view of Applicant's amendment, the previous rejections under 35 U.S.C. 112, first paragraph, for an inadequate written description of the "factor" of the claims has been withdrawn. The previous rejection under the second paragraph of 35 U.S.C. 112 has also been withdrawn. Additionally, the previous rejections under 35 U.S.C. 102 have been withdrawn given that the method of the prior art does not teach the stepwise method of the instant claims, i.e., that the pluripotent cells of the claims are first contacted with cytokine to produce immature DCs and then contacted with the compositions of the amended claims to become stable mature DCs.

4. Claims 5, 6, and 10 are objected to. It appears that in addition to the compositions of Claim 1, i.e., PBMC conditioned medium, monocyte conditioned medium, macrophage conditioned medium, and SACS, the intent of claim 5 is that the composition also includes GM-CSF. If that is the intention of the claim, Applicant is requested that the claim be amended to recite "the composition further comprises GM-CSF".

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6 and 10-12 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at

the time the application was filed. This is a new matter rejection.

As set forth previously, the specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, a method wherein the maturation factor is present in "macrophage conditioned medium" as recited in Claim 1.

Applicant indicates that support for the term can be found at page 22, lines 23-25 of the specification.

A review of the specification reveals that the term "macrophage conditioned medium" is disclosed just once (at page 22). This disclosure, however, is not in the context of the claimed method. First, the context is only one wherein DCs grown for 7 days in GM-CSF and IL-4 are then matured in "macrophage conditioned medium". Clearly, this disclosure is more limited in scope than are the instant claims (wherein there are no limitations on the cytokines or timing, except that they be sufficient). Second, the disclosure is only in a context of producing mature DCs and not the stable mature DCs produced by the claimed method. Note that this second issue is a critical component of the claimed invention.

7. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification,
while being enabling for,
a method comprising contacting the pluripotential cells having the potential of expressing either macrophage or dendritic cell characteristics with GM-CSF and IL-4 for a time sufficient to produce immature dendritic cells …,
does not reasonably provide enablement for,
a method comprising contacting the pluripotential cells having the potential of expressing either macrophage or dendritic cell characteristics with one or more cytokines for a time sufficient to produce immature dendritic cells ….

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir.

1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

It is well-established in the immunological arts that different cytokines have different biological functions and activities. See, for example, Janeway et al. wherein it is shown that cytokines have functions ranging from T cell growth characteristics (e.g., IL-2) to anti-neoplastic activities (e.g., OSM). Interestingly, some cytokine activities are context dependent, e.g., whereas IFN-β is sometimes anti-viral, newer data reveals that in the context of a multiple sclerosis patient IFN-β is immunosuppressive. See also Cohen et al. for a review discussing the diversity of cytokine function.

A review of the specification shows that just a single combination of cytokines was used in all experiments, GM-CSF and IL-4. Indeed, no other cytokines or combinations thereof are even disclosed. Clearly the disclosure of this single specific combination of cytokines is not commensurate in scope with the "one or more cytokines" of the instant claims.

For the above reasons, the skilled artisan would not reasonably expect any cytokine or combination thereof to prove effective in the claimed method. Absent any additional guidance, the skilled artisan is left with only a method of trial and error in determining which cytokines or combinations thereof would prove effective in the claimed method. As methods of trial and error provide no particular expectation of success

with any particular cytokine or combinations thereof, the method of the instant claims is considered to comprise undue experimentation.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

10. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

11/22/08
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER